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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/284,683	06/24/1999	GREGOR CEVC	500.1007	2670
21874	7590	06/24/2004	EXAMINER	
EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205			KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER
			1615	
DATE MAILED: 06/24/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/284,683	Applicant(s) CEVC, GREGOR	
	Examiner Gollamudi S Kishore, PhD	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-33 and 49-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-33 49-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The filing of RCE dated 4-7-04 is acknowledged.

Claims included in the prosecution are 22-33 and 49-92.

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 22-33 and 92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear as to what applicant intends to convey by 'if there is a solubilizing point' in claim 22 (step e); if there is a solvent, then won't there be a solubilizing point?

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments only explain the relative solubilities of the two components in the composition and does not address the issue raised by the examiner. According to applicant's own statements lines 1-4 of the last paragraph on page 13 of the response show that the droplets will solubilize if too much of the more soluble component is added. It is therefore, logical to infer that there will be a solubilizing point for any substance or solvent.

It is also unclear what the expression 'the reference particles are water molecules' in step f is intended to convey. One molecule of any compound cannot be seen by naked eye or even electron microscope. How can these be considered as particles? The claim steps are still very confusing in spite of the amendments.

Claim 92 which is dependent from 22 recites 'wherein the transfersomes are produced by a method selected from ----'. Claim 22 however, deals with a method of production of transfersomes. Is the step recited in claim 92 an additional step?

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 53-91 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-35 of U.S. Patent No. 6,165,500. Although the conflicting claims are not identical, they are not patentably distinct from each other because for the following reasons. Instant claims are drawn to treatment of a mammal by administering the same transfersomes to the skin or mucous membrane of the mammal. Since the transfersomes have to be transported through the

skin as claimed in patented claims, instant claims encompass the patented claims.

Instant claim 53 is generic with respect to the amount of the lipid and the lipid: surfactant ratios in patented claims.

3. Claims 22-33 and 49-92 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 69-87 and 101-103 of copending Application No. 10/357,618. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 22-33 and 92 and the claims 69-79 are drawn to a method of preparation of same transfersomes; instant claim language does not exclude the presence of the third substance in the method of preparation and the generic claim 69 in said copending application encompasses instant molar amounts. Instant claims 49-91 are drawn to a method of treatment using the transfersomes and thus encompasses 'a method for generating a therapeutic effect on a warm blood creature applying transfersomes; as stated above, instant claim language does not exclude the presence of the third substance in the composition used in the method of generating a therapeutic effect in the claims of said copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 U.S.C. § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 22-33 and 49-92 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 475 160 of record (English equivalent, US 6165,500).

EP discloses instant composition (transfersomes) containing a drug, amphiphilic lipids (such as PC and PG) and a surfactant (oleic acid) in instant amounts and a method of preparation (see the entire document and the English equivalent). The Examples 32-39 show the amounts of the lipids and surfactant, which appear to fall within the claimed limits. Although the reference does not explicitly recite the claimed steps such as selecting the lipids, adopting the composition by adjusting the amounts of the soluble component and adjusting the concentration of the lipid, since one cannot come up with specific amounts of the components as seen in example 32-39 of the reference without experimentation, the claimed steps are deemed to be implicit.

Applicant's arguments have been fully considered, but are found to be persuasive. Applicant argues that the present preparations form enveloped droplets that enclose an active agent. These droplets according to applicant are essentially formed of two amphiphilic components and that the insertion of the more soluble second

component destabilizes the droplets and make them ultra deformable. Further, according to applicant if too much of the second component is added, then the droplets will solubilize (solubilization concentration) and this concentration must not be reached. Therefore, according to applicant the second component is added in an amount less than 0.1 mole percent and that EP reference describes transfersomes having a content of surface active agent corresponding to 0.1 to 99 mole % of the content of the substance representing the solubilization concentration of the droplets. These arguments are not found to be persuasive. First of all, the prior art and instant invention deal with the same transfersomes and method of preparation. Secondly, as admitted by applicant himself, 0.1 to 99 % in 6,165,500 (EP) referred to by applicant refers to surface-active agent and according to the examples in 6,165,500 (EP) (Examples 32-39) the surface-active agent is oleic acid and not the amount of the second amphiphilic component in EP, which is a phospholipid. Applicant has not shown that the second component in these examples is not in claimed amounts. Thirdly, instant independent claim 53 does not recite any specific mole percentages. Furthermore, US 6,165,500 discloses the same amphiphilic phospholipids on columns 6-7 and 14 as disclosed in instant specification on pages 12-16.

Claim Rejections - 35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 22-33 and 49-92 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 475 160 cited above (English equivalent, US 6,165,500).

As pointed out above, EP teaches the same transfersome composition containing a drug, combination of amphiphilic lipids and a surfactant in instant amounts and a method of preparation. It is unclear whether the reference teaches all the instant functional parameters and mole percentages (since they are given in terms of weight). In case they are different, in the absence of showing the criticality, they are deemed to be parameters manipulatable by an artisan to obtain the best possible results.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant's arguments once again center on the differences in the mole percentages in the prior art and in instant invention. These have been addressed above. Assuming the amounts of the second amphiphilic substance are different and if the mole percentages of 0.1 to 99 % refers to the second amphiphilic component, it is the examiner's position that adjusting the amounts of this component is a manipulation of the prior art's teachings to obtain the best possible results. The lower limit in EP (US

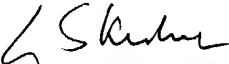
6,165,500) is 0.1 mole percent and based on the discussions of the required elasticity of the transfersomes and the criteria of the lipid- surfactant ratios and the solubilization concentrations on column 2, line 56 through col. 3, line 4 and col. 4, lines 15-56, one of ordinary skill in the art would manipulate the basic teachings of the prior art with the expectation of obtain the best possible transfersomes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1615

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK